Page 76, delete lines 1-20.

Page 77, delete lines 1-15.

Page 78, delete lines 1-6.

Page 80, delete lines 1-25.

Page 81, delete lines 1-9.

Page 82, delete lines 1-5.

Page 83, delete lines 1-15.

Page 84, delete lines 1-4.

Page 85, delete lines 1-8.

Page 86, delete lines 1-5.

Page 87, delete lines 1-4.

Page 88, delete lines 1-6.

Figures

REMARKS

Reconsideration and allowance of the above-referenced application, as amended, are respectfully requested.

The second of two pages numbered 71 has been deleted; this extraneous page was inadvertently incorporated into the specification.

The specification has been amended to present the citations of published works in the more customary style, namely by incorporation directly into the text where cited.

The specification has also been amended so that the description of the Figures are placed under the section entitled

"Brief Description of the Drawings" rather than under the Figures. No new matter has been entered into the specification.

Claims 1-3, 6 and 7 have been amended. New claims 16-19 have been added. Support for claim 16, 18 and 19 may be found in the sequences disclosed in the specification in Figure 3. Support for the DNA segment called clone T-11 recited in claim 17 may be found in Figure 2 and pages 18, line 8, through page 20, line 6.

Support for the changes made on page 15, line 12 corresponding to Figure 3 on page 15, line 26 corresponding to Figure 7, and on page 16, line 3, corresponding to Figure 8 may be found on page 18, lines 8-23, page 44, lines 3-9 and page 45, lines 4-10, which discloses the specific embodiment of the claimed invention.

These amendments rectify the Examiner's concerns regarding the TR_4 and T_{11} clones and the sequence depicted in Figure 3. The Examiner is correct when stating in the previous office action on page 4 second paragraph that Figure 3 is the DNA sequence for the TR_4 cDNA clone. The changes made in Figure 7 and Figure 8 correspond to the cDNA T_4 and genomic T_{11} nomenclature disclosed on page 18, and also on page 44, lines 3-9 describing the expression of the "T_{11} gene product (α PGDF receptor) "utiliz[ing] M426 embryo fibroblast cells from which cDNAs of both receptors had been isolated", and page 45, lines 4-

10 describing the functional expression of the cDNA encompassing the sequences in Figure 3, (that being the TR_4 cDNA).

Objection to the Specification and Rejection of Claims 1-7 Under 35 U.S.C. 112, 1st Paragraph.

The Applicants respectfully traverse the objection to the specification and rejections of claim 1-7 under section 112, 1st paragraph.

The specification has been corrected to indicate the correct parameter of "hydropathicity" on page 15 to correspond with the graph displayed in Figure 4.

The description of the Figures have been moved to the "Brief Description of the Drawings" section following proper patent disclosure procedures.

On page 4, 1st paragraph of the Office Action, the Examiner suggests that Figures 2 and 3 are confusing and conflict with each other. In order to address the Examiner's concerns, the following explanation of the Figures are given.

In Figure 2, the genomic T11 clone has EcoR1 cloning sites of the lambda vector. Only a portion (black boxes) encompasses exons of the processed transcript. Figure 3 is the nucleotide sequence of the complete cDNA of the α PDGF receptor. It represents the sequence of the processed transcript of the entire genomic DNA of which the T11 genomic clone represents only

a portion. The cDNA has two EcoR1 sites at nucleotide position 263 and 4917. a, b and c in Figure 2 represents exons of the genomic T11 DNA clone which are present in the TR4 cDNA coding sequence as is designated in Figure 3.

The TR4 cDNA shown in Figure 3 contains all the coding sequences of the T11 genomic clone (exons a, b and c in Figure 2) and encompasses the entire cDNA coding sequence. It also contains untranslated 5' and 3' sequences as well.

The TR4 cDNA clone shown in Figure 3 encompasses all of the partial cDNAs including HF1, HB6 and EF17. Its sequence is fully enabling for the generation of specific probes whose sequences specifically detect α as opposed to ß PDGF receptor. The disclosure provides a schematic comparison of the two receptor sequence in Figure 4.

In response to the Examiner's question on page 4, paragraph 2, of the Office Action, the Figure 3 sequence is directed to the T4 cDNA clone as the Examiner correctly noted is disclosed on page 18, lines 19-23 of the specification.

The sequence of the genomic T11 clone is not disclosed in the specification. However, a deposit of the T11 clone and the appropriate declaration regarding the public availability upon issuance of the Patent Application will be shortly submitted (see next section also). The specification will show the accession number given to the T11 clone.

On page 4, third paragraph, through the top of page 5 of the Office Action, the Examiner requests deposits of the hybridization probes or antibodies that differentiate the α and ß forms of PDGF receptor in order to enable the claims that are directed to PDGF receptor not limited to the specific sequence shown in Figure 3.

In response to the Examiner's requests, the applicants are currently preparing the deposits the DNA probes that discriminate the α and ß receptor transcripts. These probes are described in Appendix A attached to this amendment. The deposited DNA probes and the appropriate declarations regarding their public availability upon issuance will shortly be submitted in a supplemental declaration. The accession number given to these probes will also be indicated in the specification.

Regardless of forthcoming deposited clones, applicants submit that enablement for antibodies that distinguish the α and ß forms of PDGF receptor are already disclosed in applicants' instant application. One α PDGF receptor peptide sequence was used to immunize rabbits and a specific polyclonal antibody was developed against α PDGF receptor (see Figure 7). The sequence is disclosed in the specification on page 25, lines 3-10, and corresponds to the amino acid sequence given in Figure 3. This stretch of 15 amino acids begins at amino acid residue

corresponding to 967 and extends to residue 981 as shown in Figure 3.

Furthermore, page 25, lines 18-24, discloses the production of specific antisera. The specific peptide above is chemically synthesized and conjugated to a carrier such as thyroglobulin and injected into rabbits with complete Freund's adjuvant according to standard methods well known in the art in order to produce anti-T11 antibodies. The anti-HPR antibodies (antibodies raised against the PDGF receptor type ß form protein) are made with the corresponding ß type specific peptides using the same method as above (page 25, line 26-page 26, line 2).

The specification also describes the ligand binding differences of the antibodies distinguishing the protein products expressed in cells transfected with either the PDGF α or ß receptor cDNAs (see Figure 8).

Therefore, in view of the forthcoming deposits and enabling disclosure, it is respectfully requested that the Section 112, 1st paragraph objection to the specification has been obviated and rejection of claims 1-7 be withdrawn.

Rejection of Claims 1-6 Under 35 U.S.C. 112, 1st Paragraph.

The applicants respectfully traverse the rejection of claims 1-6 under Section 112, 1st paragraph, as the disclosure being allegedly enabling only for claims limited to compositions

containing a DNA segment having a sequence of Figure 3. Applicants submit that this rejection is overcome by the forthcoming deposit of the requested DNA clones to enable claims to DNA segments other than those defined by the sequence of Figure 3. Furthermore, applicants point to their enabling disclosure of specific antibodies that distinguish DNA segments that encode either α or ß PDGF receptor protein (see previous arguments).

Accordingly, in view of applicant's forthcoming submission of deposits and a declaration regarding the public availability of the deposited material upon issuance of the application and enabling disclosure of antibodies that distinguish α and ß DNA segments that encode PDGF receptor protein, it is respectfully requested that the Section 112, 1st paragraph, rejection of claims 1-6 be withdrawn.

Rejection of Claims 1-7 Under 37 U.S.C. 112, 2nd Paragraph.

The applicants respectfully traverse the rejection of claims 1-7 under Section 112, 2nd paragraph, for the following reasons.

Again, the applicants respectfully submit that the confusion the Examiner has with regards to the compositions of T11 and TR4 have been previously clarified in the discussion

found in the objection to the specification and rejection of claims 1-7 shown above.

In metes and bounds of the DNA segment of claims 1-6 are defined as now amended to recite the "DNA segment consisting essentially of the sequences that encode the human type α platelet derived growth factor... ."

The abbreviation "PDGF" has been replaced with the complete name in the claims.

To practice the α form of PDGF receptor, the DNA probes will be deposited. The specific antibodies are believed to already be enabled in the specification (see previous discussion). Thus the question of enablement to practice the α form of PDGF receptor as brought forth by the Examiner on page 7, paragraph 4, has been addressed.

Claim 7 has been amended so as to claim the α receptor protein "comprising" the amino acid sequence defined in Figure 3.

In view of the above comments and amended claims, it is believed that the Section 112, 2nd paragraph, rejection has been overcome and the rejection of claims 1-7 be withdrawn.

Rejection of Claims 1, 3 and 7 Under 35 U.S.C. 101.

The applicants respectfully traverse the rejection of claims 1, 3 and 7 under Section 35 U.S.C. 101 as allegedly being directed to non-statutory subject matter.

The Examiner raises the argument that the claimed DNA segment in protein leave a naturally occurring DNA in protein.

Applicants have amended the claims as to recite "a DNA segment consisting essentially of a sequence that encodes" a specific DNA and "a substantially pure form" of the protein that being the human α platelet derived growth factor receptor to avoid recitation on naturally occurring DNA and protein compositions.

In view of the above, it is respectfully requested that the revisions of the claims obviate the rejection and the rejection made under Section 35 U.S.C. 101 be withdrawn.

Rejection of Claims 1, 3 and 7 under 35 U.S.C. 102(a).

The applicants respectfully traverse the rejection of claims 1, 3 and 7 under Section 102(a).

The applicants are in a position to swear behind the published date of the Gronwald et al. and Heldon et al. references. An appropriate 1.131 declaration is submitted herewith copies of relevant pages from the laboratory notebooks of the applicants to provide evidence of conception of the invention and reduction to practice performed in this country prior to the publication of the references.

In addition, the rejection made under 35 U.S.C. 102(a) as being anticipated by either Gronwald et al. or Heldon et al.

or 103 as being obvious over Gronwald would fail in view of the arguments presented below.

Both references cited disclose ligand binding results consistent with the existence of two PDGF receptor subtypes, but each reference cannot determine whether they are differently processed products of the same gene or products of different genes. For example, in the discussion section of Gronwald et al., the authors are not sure what PDGF receptor they have isolated (in fact applicants demonstrate in the instant invention that it was ß receptor). Furthermore, they are uncertain if a second distinct gene product exists for other PDGF receptor classes or alternatively if postranslational modifications are responsible for generating PDGF receptor classes. Thus, the references do not anticipate the claimed invention since the references do not teach the composition of the claimed invention.

Neither reference, nor any reference prior to applicants claimed invention, provide any structural or sequence data or any DNA probes or antibodies able to identify or specifically detect the α PDGF receptor, which applicants disclose and claim as their invention to be the product of a different gene.

Furthermore ligand binding data published by various groups including the cited references were also in conflict, but there was evidence consistent with the 1988 published reports that possible subtypes of the two receptors existed. Again,

these findings did not disclose whether the possibility of the two receptors would reflect different process products of a single gene, or whether two genes existed which encode two distinct receptors. In fact, nothing published prior to applicants disclosure identifies or defines the alpha receptor at any structural level.

Therefore, each reference does not anticipate the α receptor protein because at the time of the claimed invention, the α form of the PDGF receptor and protein were not known. The α PDGF receptor form disclosed in the references are not the same subject matter defined by applicants in the instant invention.

Therefore, for the reasons discussed above, it is believed that the claims are not anticipated by the references and that the rejection should be withdrawn.

Rejection of Claims 2 and 4-6 Under 35 U.S.C. 103.

Applicants submit that claims 2 and 4-6 are not rendered unpatentable over Gronwald et al.

Gronwald et al. discloses the cloning of the ß form of the PDGF receptor as indicated by the Examiner. However, Gronwald et al. does not disclose or suggest the α form of the PDGF receptor DNA segment or corresponding protein. As argued above, Gronwald et al. does not disclose or suggest the α receptor at any structural level that applicants have identified

and defined. Furthermore, Gronwald did not disclose whether a possible second receptor would reflect different processed products of a single gene or whether it would exist as two genes encoding two distinct receptors.

For example, the predicted ligand binding domain of the α PDGF receptor cloned by applicants is very different from that of the human PDGF receptor of Gronwald. It would not be predicted, based upon its predicted sequence, that it would bind a common ligand PDGFBB at similar high affinity (see the sequence comparisons of related receptors in Figure 4). Other related receptors in Figure 4 bind completely different ligands, unrelated to any of the PDGF ligands.

The applicants approach for identifying and cloning the genes and cDNA of the α PDGF receptor are completely independent and different from those initiated prior to the claimed invention. Using a cDNA probe of a different member of a family of related receptors, (c-*fms*/CSF-1 receptor), whose ligand is completely different from the PDGF, a new PDGF receptor gene was unexpectly found.

At the time of the claimed invention, evidence published by Williams and co-workers indicated that the mouse PDGF receptor (later designated as the mouse ß PDGF receptor), bound all forms of PDGF. There was no expectation of the existence of another PDGF receptor based on these methods, and certainly there was no

expectation of a distinct gene encoding a new PDGF receptor based on these methods nor the methods disclosed by Gronwald et al.

Thus, applicants assert that there is no teaching, suggestion or motivation in Gronwald to make the presently claimed invention obvious.

Based on the foregoing analysis, the applicants respectfully submit that the rejection of claims 2 and 4-6 under Section 103 has been overcome. As shown above, Gronwald et al. teaches away from the claimed invention with respect to the finding of a distinct new PDGF receptor gene. It is respectfully submitted that the claimed invention is fully patentable.

In conclusion, it is believed that the subject application is in condition for allowance and notice to that effect is respectfully requested.

Respectfully submitted,

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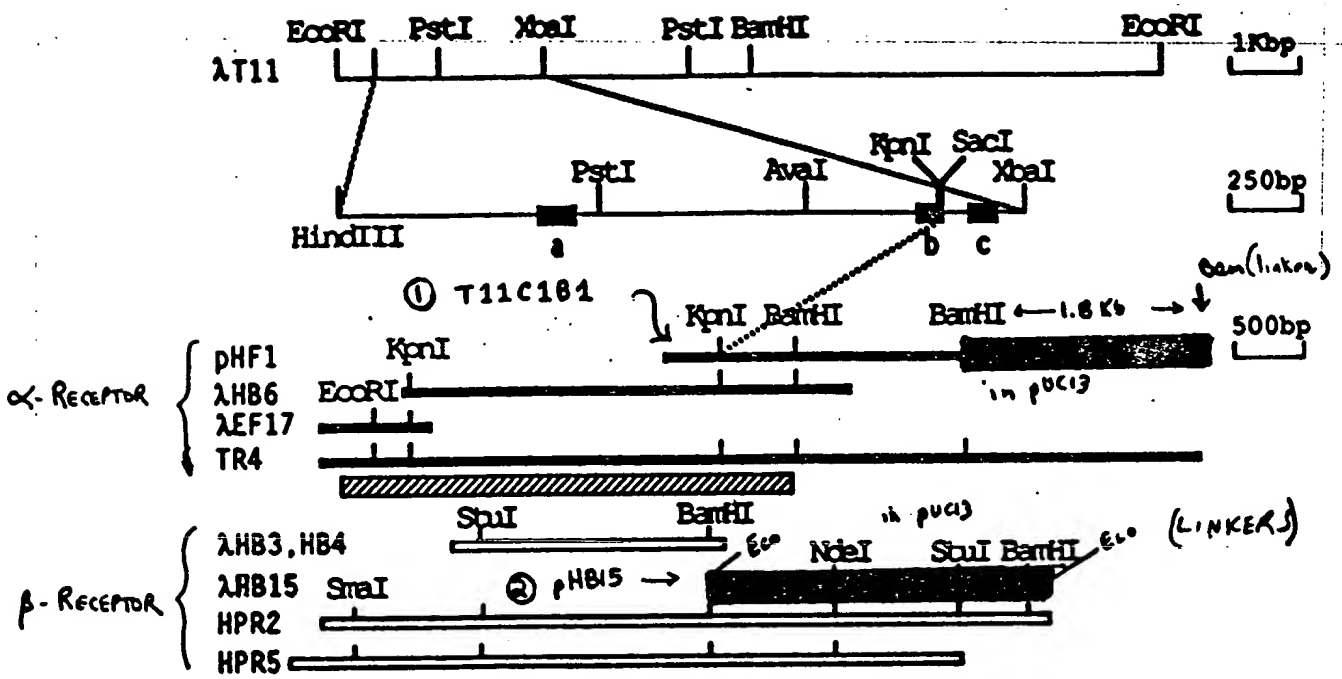
APPENDIX A



DEPOSITED PROBES

1. T11C1B1 represents the 3' end of ∝ PDGF receptor

2. pH815 represents the 3' end of ß PDGF receptor